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Dr. M Sundareshwaran
Post Graduate, Department of General Medicine, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, Tamil Nadu, India

Dr. Saritha K Narayanan
Associate Professor, Department of General Medicine, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, Tamil Nadu, India

Dr. M Ramakrishna Rao
Professor, Department of General Medicine, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, In Tamil Nadu, India

Corresponding Author:
Dr. Saritha K Narayanan
Associate Professor, Department of General Medicine, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, Tamil Nadu, India

Estimation of serum Vitamin D level in hypertension and hypertension related complications

Dr. M Sundareshwaran, Dr. Saritha K Narayanan and Dr. M Ramakrishna Rao

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Abstract
Background: India with population of around 1.38 billion harbours nearly 200 million[1] hypertension patients. Hypertension is an important non-communicable disease with multifactorial biological aspects for its pathogenesis. Many recent analytical studies supported the evidence of low serum vitamin D level in pathogenesis of hypertension. Our objective was to estimate serum vitamin D level in patients with hypertension and hypertension related complications.
Aims & Objectives: 1. To estimate serum Vitamin D level in Essential Hypertension and Hypertension related complications. 2. To establish the relationship between serum Vitamin D level and Hypertension and hypertension related complications.
Materials & Methods:
Design: Hospital based Observational study
Place of Study: Department of General Medicine
Study Population: Cases attending RMMCH OPD during the study period will be screened for hypertension and hypertension related complications.
Sample Size: 100
Results: It has been observed that in this study serum vitamin D level is low in hypertension patients and also, the lower level correlated with hypertensive complications like retinopathy, nephropathy and cardiac complications.
Conclusion: The study results reveals that low serum vitamin D level is present in significant number of study populations. Also the low serum vitamin D level correlated with hypertension related complications.

Keywords: Systemic hypertension, retinopathy, nephropathy, left ventricular hypertrophy, renin angiotensin system

Introduction
Vitamin D is a steroid molecule and lipid soluble vitamin, mainly produced by the skin and absorbed from the gut. Its main role is in the control of bone metabolism and calcium and phosphorus homeostasis. Vitamin D is a part of the Calcium-Vitamin D – Parathormone endocrine axis. It is crucial for calcium metabolism and its homeostasis. Vitamin D deficiency has been traditionally associated with poor bone growth and development manifesting as rickets in children and osteoporosis in adults. In recent years much emphasis has been given to the role of vitamin D in areas beyond those traditionally known. During the last two decades new researches and data are showing that vitamin D deficiency could be a risk factor in many chronic diseases like hypertension, diabetes mellitus [2], dyslipidemia, cardiovascular disease, some cancers, auto immune disease (Crohns [3] disease, Multiple sclerosis [4]) and tuberculosis.
Hypertension is a polygenic and multifactorial disease involving many pathways and mechanisms. In India, with a population of more than one billion, estimated number of patients may be around 200 million [1]. There is a significant morbidity, mortality and economic burden on a developing country like India.
Many epidemiological studies have demonstrated an inverses relationship between vitamin D levels and blood pressure. Studies in India have demonstrated that the level of vitamin D in the population is low and there is high prevalence of chronic diseases like hypertension, diabetes, cardiovascular disease [2].

Aims & Objectives

1. To estimate serum Vitamin D level in Essential Hypertension and Hypertension related complications.
2. To establish the relationship between serum Vitamin D level and Hypertension and hypertension related complications.

Patient selection

The cases attending RMMCH OPD are screened for hypertension and hypertension related complications. Based on inclusion and exclusion criterias, patients are enrolled in this study.

Inclusion criteria

1. Male - Above 18 years, Female - Above 18 years
2. Hypertensive Retinopathy

Based on fundus examination examined with *Direct Opthalmoscope* and with following findings;

a. Grade 1 - Mild to moderate narrowing or sclerosis of the smaller arteriole
b. Grade 2 - Moderate to severe narrowing of smaller arterioles

Exaggeration of light reflex
Changes at the arteriovenous crossing

c. Grade 3 - Retinal arteriole focal constriction

Prominent arteriovenous crossing,
Retinal edema
Cotton wool spots
Flame shaped haemorrhages.

d. Grade 4 – Grade 3 plus features of Papillary edema.

3. Hypertensive Renal Disease

Based on applying laboratory values of serum creatinine in mg/dl and age in years in the following formula eGFR (ml/min/1.73m^2) = 175*(Sr cr)$^{-1.154}$*(age)$^{-0.203}$*0.742(if female)*1.212(if black) and eGFR is obtained

4. Hypertensive Cardiac Disease

Based on Electrocardiographic findings suggesting Left ventricular hypertrophy

Sokolow-Lyon Voltages: SV1 + RV5 > 3.5mV, RaVL >1.1mV

Exclusion criteria

1. Diabetes Melliteus: HBA1C - >7%
2. Thyroid Function Tests: Based on laboratory specific cut off values. Patients having T3, T4 & TSH values more or less are excluded from the study.

Total T3	2.8-7.3 pmol/L
Total T4	8.4-22.5 pmol/L
TSH	0.4-5.5 microIU/ml

5. Patients on Vitamin D and other unknown nutrition supplements: Based on Patients history or confirming the intake if the Patient is having drug by himself/herself.
6. History of any Gastrointestinal Surgeries
7. Based on available past medical records or presence of abdominal scar in clinical examination.

Study pattern

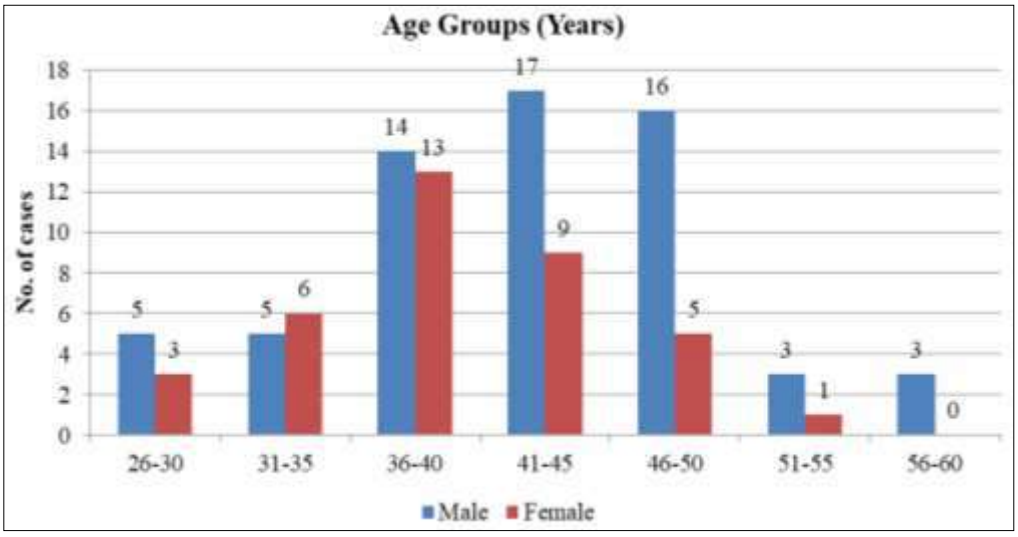
Based on inclusion and exclusion criteria, patients were being enrolled in the studies and they are estimated with serum vitamin D levels. Depending on patients serum vitamin D levels, patients are divided into sub groups as normal (>30ng/dl), insufficiency (20-30ng/dl) and deficiency (<20ng/dl). Within each subgroups patients are screened and evaluated for hypertension related complications like Hypertensive retinopathy, Hypertensive kidney disease and Hypertensive cardiac disease. Serum vitamin D level and in relation with hypertension and hypertension related complications were studied using statistical analysis.

Results

Based on the observational study conducted following results have been obtained and analysed statistically.

Table 1: Distribution of study population according to their age groups

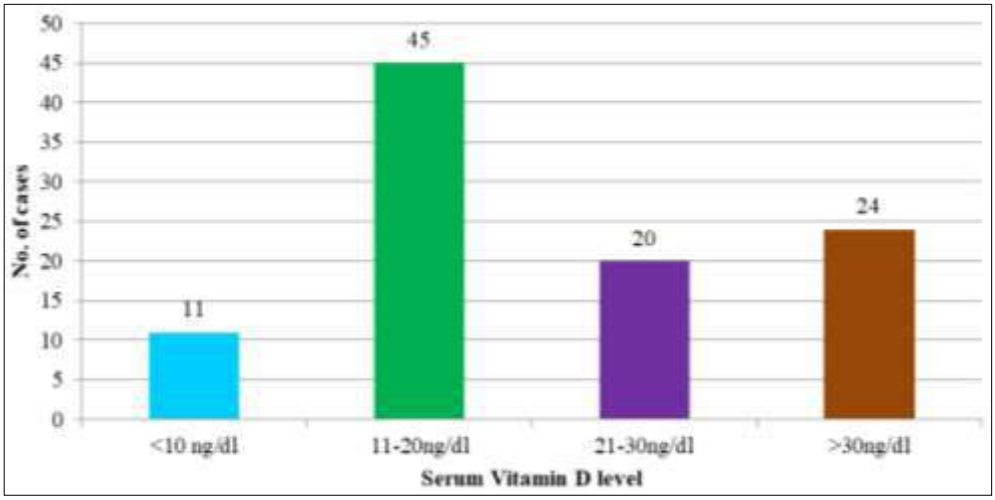
Age groups (years)	Male	Female	Total
26-30	5	3	8
31-35	5	6	11
36-40	14	13	27
41-45	17	9	26
46-50	16	5	21
51-55	3	1	4
56-60	3	-	3
Total	**63**	**37**	**100**



Graph 1: Distribution of study population according to their age groups

Table 2: Distribution of study population according to serum Vitamin D levels

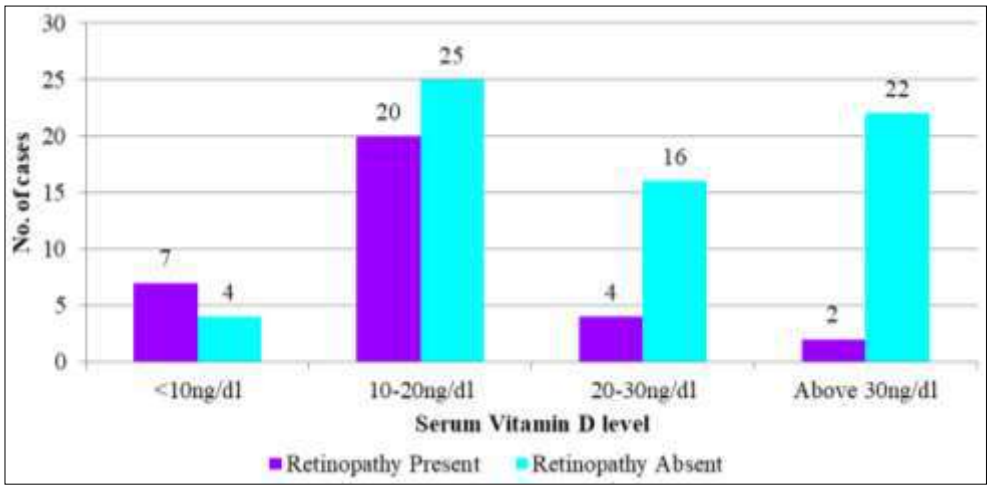
Serum Vitamin D	Number of cases	Percentage
<10 ng/dl	11	11
11-20ng/dl	45	45
21-30ng/dl	20	20
>30ng/dl	24	24
Total	**100**	**100**



Graph 2: Distribution of study population according to serum Vitamin D levels

Table 3: Serum Vitamin D level and retinopathy

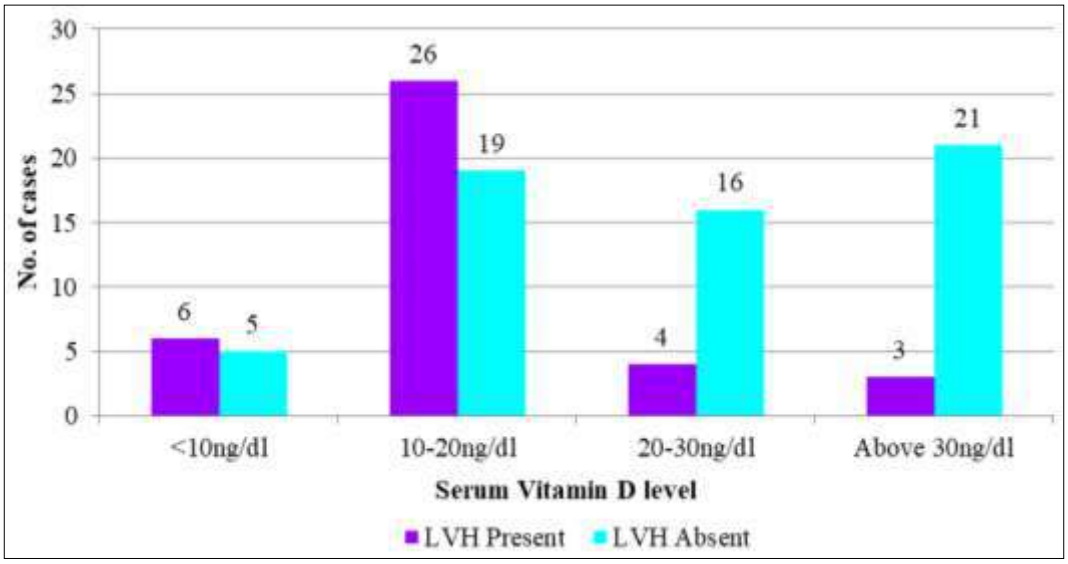
Serum Vitamin D	Retinopathy Present	Retinopathy Absent
<10ng/dl	7	4
10-20ng/dl	20	25
20-30ng/dl	4	16
Above 30ng/dl	2	22
Total	**33**	**67**



Graph 3: Serum Vitamin D level and retinopathy

Table 4: Serum Vitamin D level and left Ventricular Hypertrophy

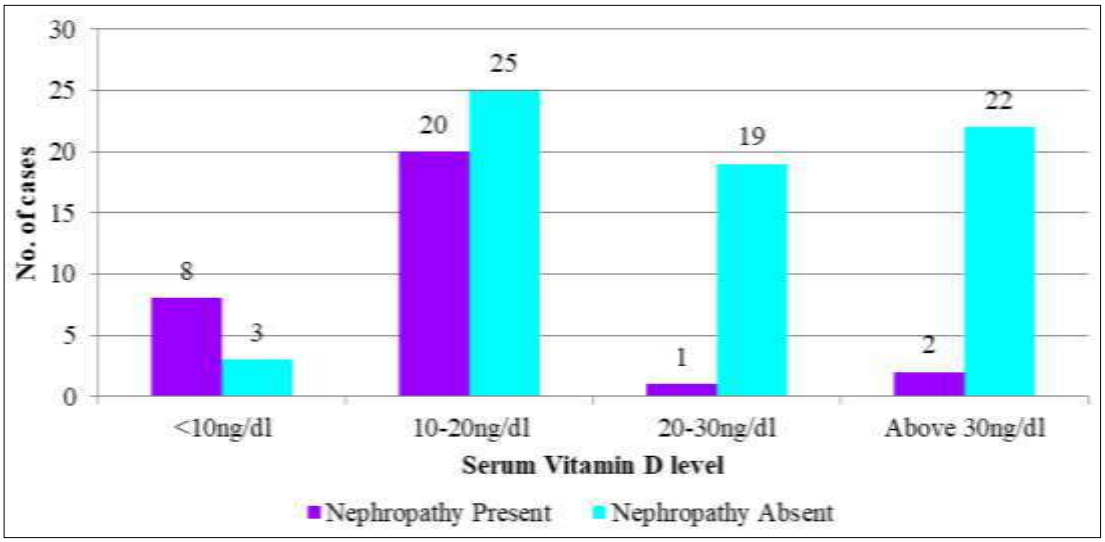
Serum Vitamin D	LVH Present	LVH Absent
<10ng/dl	6	5
10-20ng/dl	26	19
20-30ng/dl	4	16
Above 30ng/dl	3	21
Total	**39**	**61**



Graph 4: Serum Vitamin D level and left Ventricular Hypertrophy

Table 5: Serum Vitamin D level and nephropathy

Serum Vitamin D	Nephropathy Present	Nephropathy Absent
<10ng/dl	8	3
10-20ng/dl	20	25
20-30ng/dl	1	19
Above 30ng/dl	2	22
Total	**31**	**69**



Graph 5: Serum Vitamin D level and nephropathy

Table 6: Frequency distribution of serum vitamin D level in Retinopathy patients

Serum Vitamin-D Levels (ng/dl)	Study subjects				Total	
	Retinopathy present		Retinopathy Absent			
	Frequency	%	Frequency	%	Frequency	%
<10	7	21.2	4	6	11	11
10-20	20	60.6	25	37.3	45	45
20-30	4	12.1	16	23.9	20	20
>30	2	6.1	22	32.8	24	24
Total	33	100	67	100	100	100

$\varkappa^2 = 15.469$, df=3 p=0.014 (high Significant)

Table 7: Frequency distribution of serum vitamin D level in CRF patients

Serum Vitamin-D Levels (ng/dl)	CRF present		CRF Absent		Total	
	Frequency	%	Frequency	%	Frequency	%
<10	8	25.8	3	4.3	11	11
10-20	20	64.5	25	36.2	45	45
20-30	1	3.2	19	27.5	20	20
>30	2	6.5	22	32	24	24
Total	31	100	69	100	100	100

$\varkappa^2$ =24.842, df=3 p=0.000017 (highly Significant)

Table 8: Frequency distribution of serum vitamin D level in LVH patients

Serum Vitamin-D Levels (ng/dl)	Study subjects				Total	
	LVH present		LVH Absent			
	Frequency	%	Frequency	%	Frequency	%
<10	6	15.4	5	8.2	11	11
10-20	26	66.7	19	37.3	31.2	45
45	4	10.2	16	26.2	20	20
>30	3	7.7	21	34.4	24	24
Total	39	100	61	100	100	100

$\varkappa^2$ =17.907, df=3 p=0.0004 (highly Significant)

Based on the obtained results it is concluded that, among 100 hypertensive patients screened for complications 24 had normal, 20 had insufficient and 56 had deficient serum vitamin D levels. Number of patients in each subgroup were analysed for respective complications in study. It is observed that low serum vitamin D level correlated with severity of complications. By applying statistical analysis, positive correlation has been established between low serum vitamin D level in hypertension and hypertension related complications.

Among 33 retinopathy complicating patients 4 of them had serum vitamin level in insufficient range and 27 of them in deficient range with highly significant p value of 0.0014.

Among 39 LVH complicating patients, 4 of them had insufficient vitamin D level and 32 of them in deficient range with highly significant p value of 0.0004.

Among 31 nephropathy complicating patients, only one of them had insufficient level and 28 of them in deficient range of serum vitamin D with highly significant p value of 0.000017.

Discussion

Systemic hypertension is a major risk factor for cardiovascular, cerebrovascular, renovascular and retinovascular disease. The incidence and prevelance of hypertension is increasing resulting in increased mortality and morbidity. Many recent studies show that vitamin D plays a key role in influencing various parameters that regulate high blood pressure via various pathways including endothelial cell function, proliferation of vascular smooth muscle cells, regulation of renin-angiotensin pathway [5]. And vitamin D also play an important role in regulation of blood pressure [8] via increased intracellular calcium leading to decreased renin activity [6, 7].

Vitamin D plays a role in regulating vascular tone by influencing the concentration of calcium in vascular smooth muscle cells [5]. Intracellular calcium accumulation results in an inhibition of renin secretion in juxtaglomerular cells.

Vitamin D is a proximal inhibitor of RAS and inhibition of 1, 25 (OH) vitamin D synthesis results in an increase in renin expression and increase in 1, 25 (OH) vitamin D synthesis results in renin suppression [5]. More recently a study showed 25 (OH) D is inversely associated with plasma renin concentration [8].

In a large study involving blacks in United States - Third US National Health and Nutrition Examination Survey[9] (NHANES III) - demonstrated low serum vitamin D level in hypertension patients. However some studies related serum vitamin D level related to systolic blood pressure but donot predict the future hypertension [10].

In our study there is a significant correlation between low levels of serum vitamin D level and hypertension. There is also a significant correlation between serum vitamin D level and hypertension related complications.

Conclusion

The current study showed hypertensive patients had lower levels of serum vitamin D and lower serum vitamin D level correlated well with hypertension related complications. Hence Vitamin D deficiency is associated with high blood pressure which is supported by several biological pathways.

However, randomized clinical trials and their meta-analyses have yielded inconclusive results. Large randomized trials focusing on patients with severe vitamin D deficiency and hypertension are needed before vitamin D can be recommended for the prevention or treatment of hypertension.

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